B1 cont'd

wherein the common region is shared by each of the oligonucleotides in the set, and is of a sufficient length to serve as a unique priming site for amplifying nucleic acid molecules that comprise the sequence of nucleotides that comprises the common region.

**REMARKS**

A check for the fee for two month extension of time accompanies this response. Any fees that may be due in connection with filing this paper or with this application may be charged to Deposit Account No. 50-1213. If a Petition for Extension of time is needed, this paper is to be considered such Petition.

Claims 1-37, 49-54, 93-95 and 99 are pending in this application. Claims 38-48, 55-92 and 96-98 are cancelled herein. Applicant reserves the right to file divisional applications to the cancelled subject matter. It is noted that the restriction requirement is defective because claims 95-98 were not included in any group. It is respectfully submitted that that claim 95 belongs in group I and claims 96-98 belong in groups VIII and IX, which as discussed below, should be rejoined.

**Traversal of the Requirement for Restriction**

Applicant respectfully traverses the requirement for restriction as between Groups I and III, groups I and II and also groups VIII and IX. It is respectfully submitted that groups III and I and group I and II are each related as a combination/subcombination for which a showing of two-way distinctness is required. Groups VIII and IX are related as a genus/species. Also the claims in groups VIII and IX are cancelled herein, arguments for rejoinder are presented because a divisional application with the claims in these groups has been filed under separate cover.

**Groups I and III**

Inventions that are related as a combination and subcombination are distinct and restriction may be proper **only if** it can be shown that the combination as claimed does not require the particulars of the subcombination

as claimed for patentability **and** that the subcombination has utility by itself or in other combinations. See MPEP 808.05(c).

In this instance Group III is directed to a system (the combination) that comprises the combinations (the subcombination) of Group I. Claims 49 and 50 and claims dependent thereon are directed to systems for sorting collections of molecules that include a combination of group I, and software for analyzing the results of the sorts. If the combinations of group I are deemed novel and unobvious, the systems of Group III are necessarily novel and unobvious. Therefore, the systsems of Group III (the combination) and the combinations of Groups I (the subcombinations) are not distinct.

If the claims are restricted into these two groups, applicant ultimately could be granted two patents, one that includes claims directed to the combinations of claim 1, and another with claims directed to systems that include the combinations of group I, that expire on different dates. If the claims to the the subcombination (group I) issued first, a later issuing patent encompassing the systems (Group III) (combination) could not be held to constitute obvious-type double patenting over the earlier issuing patent. See MPEP 806, paragraph 3, which states:

> [w]here inventions are related as disclosed but are not distinct as claimed, restriction is never proper. Where restriction is required by the Office double patenting cannot be held, and thus, it is imperative the requirement should never be made where related inventions as claimed are not distinct.

See, also MPEP 804.01, which states:

> 35 U.S.C. 121 authorizes the Commissioner to restrict the claims in a patent application to a single invention when independent and distinct inventions are presented for examination. The third sentence of 35 U.S.C. 121 prohibits the use of a patent issuing on an application with respect to which a requirement for restriction has been made, or on an application filed as a result of such a requirement, as a reference against any divisional application, if the divisional application is filed before the issuance of the patent. The 35 U.S.C. 121 prohibition applies only where the Office has made a requirement for restriction. The prohibition does not apply where the divisional application was voluntarily filed by the

> applicant and not in response to an Office requirement for restriction. This apparent nullification of double patenting as a ground of rejection or invalidity in such cases imposes a heavy burden on the Office to guard against erroneous requirements for restrictions where the claims define essentially the same invention in different language and which, if acquiesced in, might result in the issuance of several patents for the same invention.

As noted above, if the combinations of Group I are deemed free of the prior art, then the systems of Group III, which include the combinations of Group I, will necessarily be fee of the prior art. Since restriction of such Groups is improper, reconsideration and withdrawal of the restriction requirement as between Group I and Group III is, therefore, respectfully requested.

**Groups I and II**

As noted, inventions that are related as a combination and subcombination are distinct and restriction may be proper **only if** it can be shown that the combination as claimed does not require the particulars of the subcombination as claimed for patentability **and** that the subcombination has utility by itself or in other combinations. See MPEP 808.05(c).

In this instance Group I, claim 26, for example, is directed to a the combination that comprises the oligonucleotides of claim 38, the subcombination, of Group II. If the claims in group II, the subcombiantion are deemed free of the art, claim in group I, the combination of roup III are necessarily free of the prior art. Therefore, claims in group I and group II are not necessarily distinct.

If the restriction requirement as between these groups I and II is maintained obviousness-type double patenting cannot be held, for example, between a patent in containing claim 26 or 42 issues and a patent containing claim 38 or 99.

**Gr ups VIII and IX**

Group VIII, claims 67-74 is directed to a method for screening a nucleic acid library; and group IX, claims 75-90 is directed to, drawn to a method for nested sorting.

The methods in fact are related as a genus/species.

Claim 67 of group VIII, rewritten as an independent claim, is directed to:

A method for screening a nucleic acid library, comprising:

a) creating a tagged library by a method comprising:

incorporating each one of a set of oligonucleotides that each comprises a region $E_m$ into a nucleic acid molecule in a library of nucleic acid molecules to create a tagged library, wherein:

the oligonucleotide comprises the formula:

5'-$E_m$- 3';

each E encodes a sequence of amino acids to which a capture agent specifically binds;

each such sequence of amino acids is unique in the set; and

m is, independently, an integer of 2 or higher;

b) translating the library or a sublibrary thereof;

c) contacting proteins from the translated library or sublibrary with a collection of capture agents to produce complexes between the tagged proteins and capture agents, wherein:

each of the capture agents specifically binds to a polypeptide encoding an $E_m$; and

each of the capture agents is identifiable;

d) screening the complexed capture agents to identify those that have bound to a translated protein of interest, thereby identifying the $E_m$ that is linked to the protein of interest.

Claim 73, recites:

The method of claim 67, wherein each oligonucleotide from which the library is created comprises the formula: 5' $D_n$-$E_m$- 3'.

Claim 75 of group IX, rewritten as an independent claim, is directed to:

A method for nested sorted, comprising:

a) creating tagged collections of nucleic acid molecules by incorporating each one of the set of oligonucleotides at one end of each nucleic acid molecule to create a master collection comprising N members, wherein the oligonucleotides have the formula:

5'-$D_n$-$E_m$-3'

wherein:

each D is a unique sequence among the set of oligonucleotides and contains at least about 10 nucleotides;

each E encodes a sequence of amino acids that comprises epitope;

each epitope is unique in the set;

each epitope is a sequence to which a capture agent binds;

each of n and m is, independently, an integer of 2 or higher; and

the oligonucleotides are single-stranded, double-stranded, and/or partially double-stranded;

b) amplifying each of n samples with a primer that comprises $D_n$ to produce n sets of amplified nucleic acid reactions, wherein each reaction comprises amplified sequences that comprise a single $D_n$ and all of the $E_m$'s;

c) translating each sample to produce n translated samples;

d) contacting proteins from each translated reaction with one of n collections of capture agents to produce complexes thereof, wherein each of the capture agents in the collection specifically reacts with a sequence of amino acids encoded by an $E_m$; and each of the antibodies can be identified;

e) screening the complexes to identify those that have bound to a protein of interest, thereby identifying the $E_m$ and $D_n$ that is linked to nucleic acid molecules that encode the protein of interest.

Comparison of the steps of claim 73 and claim 75 reveals that the claim 75 primarily differs from claim 73 in that it specifies step b) and that step e) specifies that the $D_n$ as well as $E_m$ is identified. Claim 73 thus is generic to claim 75 and, thus, claim 73 and other claims in group VIII are linking claims, which must be examined with the species claims of group IX.

According to MPEP §809, when claims linking more than one group are found, the Restriction Requirement must be conditioned on:

1) specifying the linking claims; and

2) examining the linking claims with the elected group. The linking claims **must** be examined with the elected group; if the linking claims are deemed allowable, then the restriction requirement must be withdrawn and all claims directed to nonelected subject matter which depends from or includes all the limitations of the linking claims must be rejoined.

Furthermore, if the restriction requirement is maintained, these claims could issue in two patents, one that includes claims directed to the methods of

group IX and the other with claims directed to the methods of group VIII. For example if a patent with claim 75 issued first, the later issuing patent with claim 73 could not be held to constitute obvious-type double patenting over the earlier issuing patent. See MPEP 806, paragraph 3, and MPEP 804.01 noted above.

**Traversal of the election of species**

The action urges that group I and group II each encompass distinct species in which the oligonucleotides have the formulae 5'-$E_m$- 3', 5' C-$E_m$ 3', 5'-$D_n$-$E_m$- 3' and 5' C-$D_n$-$E_m$- 3'. It is respectfully submitted, however, that the "species" 5'-$E_m$- 3' is generic to the other two "species." The claims are directed to a combination that includes oligonucleotides and to oligonucleotides that comprise formula 5'-$E_m$- 3', and hence can include additional regions, such as C or $D_n$. Thus, the recited species are not "species."

* * *

In view of the remarks herein, reconsideration of the requirement for restriction and examination of all pending claims on the merits are respectfully requested.

Respectfully submitted,
HELLER EHRMAN WHITE & McAULIFFE LLP

By:_____
Stephanie Seidman
Registration No. 33,779

Attorney Docket No.:25886-1751
**Address all correspondence to:**
HELLER EHRMAN WHITE & McAULIFFE LLP
4350 La Jolla Village Drive, 6th Floor
San Diego, CA 92122
Telephone: 858 450-8400
Facsimile: 858 587-5360
email:sseidman@HEWM.com